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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/955,373	10/21/97	MOURITSEN S	P58774US3

HM22/0502

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EXAMINER	
SCHWADRON, R	
ART UNIT	**PAPER NUMBER**
1644	26

DATE MAILED: 05/02/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/955,373	Mouritsen et al.
Examiner	**Group Art Unit**
Ron Schwadron, Ph.D.	1644

☐ Responsive to communication(s) filed on _____.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *26, 28-43, and 45-53* is/are pending in the application.

Of the above, claim(s) *29-43, 48, 51, and 52* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *26, 28, 45-47, 49, 50, and 53* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Applicant's election of the species of Group A and inflammatory bowel disease in Paper No. 25 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse.

2. Claims 48,51,52 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected species. Election was made **without** traverse in Paper No. 25.

3. Claims 26,28,45-47,49,50,53 are under consideration. Claims 26 and 46 have been amended.

RESPONSE TO APPLICANTS ARGUMENTS

4. Claims 26,28,45-47,49,50,53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Claim 26 is indefinite in the recitation of "essentially preserve the overall tertiary structure" because it is unclear what this means or encompasses. It is unclear what changes to the tertiary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal structured) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "essentially preserve the overall tertiary structure".

Regarding applicants comments, the specification, pages 4 and 8 do not clarify what the term "essentially preserve the overall tertiary structure" means or encompasses because it is unclear what this means or encompasses. Regarding applicants comments about said term and preserving B cell epitopes, it is unclear what changes to the tertiary structure would or would not be encompassed by the aforementioned term. For example, it is unclear if this term encompasses changes at the physical/chemical level (eg. crystal structured) or simply functional changes (eg. still immunogenic antigen as evidenced by antibody binding by antibodies specific for unmodified antigen). If the term is interpreted as encompassing changes at the physical/chemical level, it is unclear as to what deviations from the normal crystal structure would or would not be encompassed by the term "essentially preserve the overall tertiary structure".

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 26,28,45,46 stand rejected under 35 U.S.C. 102(b) as being anticipated by Russell-Jones et al. (WO 92/05192) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered an deemed not persuasive.

Russell-Jones et al. teach T cell epitopes derived from Trat protein (see Abstract). Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. The Trat peptide has been inserted into the immunogen in such a manner as to "essentially preserve the overall tertiary structure", because the ability of the immunogen to function as an immunogen is maintained (see page 8, first complete paragraph). Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach

that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph). Said insertion would preserve flanking regions on both sides of the Trat T cell epitope. The Trat peptide has been inserted into the immunogen in such a manner as to "essentially preserve the overall tertiary structure", because the ability of the immunogen to function as an immunogen is maintained. Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans.

Regarding applicants comments about "self proteins", Russell-Jones et al. teaches that the claimed invention can be used as a vaccine in humans (see page 33) and can be used to raise antibody responses against such proteins as luteinizing hormone, somatostatin, inhibin, FSH (eg. self proteins). There is no teaching in Russell-Jones et al. that humans would be immunized with nonhuman modified luteinizing hormone, somatostatin, inhibin or FSH. The Talwar et al. abstract submitted by applicant actually discloses use of human hCG conjugated to TT. In addition, the specification, page 2, lines 22-24 discloses that Talwar et al., 1992 disclose the use of human hCG/tetanus toxoid as a vaccine in humans. Thus, use of human derived molecules in vaccines for humans was known in the art. Furthermore, the teachings of Russell-Jones et al. are not limited to methods of making immunogenic molecules more immunogenic. Russell-Jones et al. teach that, "The at least one "immunogen" which forms part of the complex *is any molecule which it is desirable to use to raise an immune response.*". Thus, Russell-Jones et al. are using the term "immunogen" to include molecules that are potentially immunogenic when conjugated to Trat. Furthermore, regarding the term "immunogen", virtually any self molecule is an immunogen if administered to another species of animal or if administered to the animal from which it was derived wherein it is administered with an appropriate adjuvant. Regarding applicants comments about insertion versus substitution, Russell-Jones et al. teach that it would be within the skill of a routineer to produce modified fusion proteins wherein Trat was included and wherein the fusion protein still had the activity of the parent molecule (see page 9). The teachings of Russell-Jones et al. are not limited to Trat insertion versus substitution and page 32 provides an example that would be applicable to any antigen. Russell-Jones et al. clearly teach substitution of Trat for amino

acid sequences found in a nonTrat molecule (see page 32). Furthermore, the teachings of page 32 are not limited to GP120 ("Using recombinant DNA technology, the "suppressor regions" in a *number of prospective vaccine proteins* including gp 120 ..."). Regarding applicants comments about whether Example 5 is enabled or not enabled, applicant has provided no evidence that said Example is not enabled. Furthermore, even if "suppressor regions" had no effect on immune responses, the Example would be no different the claimed invention, which merely discloses insertion of a exogenous T cell epitope into a molecule. Regarding applicants comments about "essentially preserve the overall tertiary structure", the Trat peptide has been inserted into the immunogen in such a manner as to "essentially preserve the overall tertiary structure", because the ability of the immunogen to function as an immunogen is maintained (see page 8, first complete paragraph). Furthermore, there is no disclosure in the specification as to what "essentially preserve the overall tertiary structure" means or encompasses, and there is no disclosure as to what changes to tertiary structure or degrees of change would or would not encompass changes that "essentially preserve the overall tertiary structure". Regarding applicants comments about whether Example 5 is enabled or not enabled, applicant has provided no evidence that said Example is not enabled.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 26,28,45-47,49,50,53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Hellman (WO 93/05810), Etlinger and prior art disclosed in the specification (page 18, last paragraph).

Russell-Jones et al. teach T cell epitopes derived from Trat protein (see Abstract). Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26 and Abstract). Russell-Jones et al. teach

that the Trat peptide is inserted such that the protein still functions as an immunogen. The Trat peptide has been inserted into the immunogen in such a manner as to "essentially preserve the overall tertiary structure", because the ability of the immunogen to function as an immunogen is maintained (see page 8, first complete paragraph). Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 32 and page 31, first incomplete paragraph). Said insertion would preserve flanking regions on both sides of the Trat T cell epitope. The Trat peptide has been inserted into the immunogen in such a manner as to "essentially preserve the overall tertiary structure", because the ability of the immunogen to function as an immunogen is maintained. Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans. Russell-Jones et al. do not teach the claimed method using TNFα. Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved using self-protein conjugated to a carrier which is recognized by T helper cells(see pages 5-12). The specification discloses that the role of TNFα in the pathogenesis of various diseases is known in the art (page 18, last paragraph). An antiTNF antibody produced by the claimed method would have been able to treat any TNF mediated disease. It would have been prima facies obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the role of TNFα was known in the art, Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved using self molecules that contain T helper epitopes and Russell-Jones et al. teach methods for inducing antibodies against self proteins using Trat modified molecules..

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in

this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 305-3014.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1800 1605

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Art Unit 1644